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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,198	03/25/2004	William A. Palmisano	41543 US 0103	8645

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PEACOCK MYERS, P.C.
201 THIRD STREET, N.W.
SUITE 1340
ALBUQUERQUE, NM 87102

EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
06/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/815,198	PALMISANO ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,7 and 10-13* is/are pending in the application.

4a) Of the above claim(s) *7, 12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments and Amendments

1. Claims 3, 7 and 10-13 are pending.

Claims 7, 12 and 13, drawn to non-elected inventions are withdrawn from examination.

Claims 10 and 11 have been amended.

Claims 3, 10 and 11 are examined on the merits.

Withdrawn Objections

Specification

2. The disclosure is no longer objected to because Applicants have submitted an amendment removing an embedded hyperlink and/or other form of browser-executable code, see Remarks submitted November 28, 2007, page 6.

Claim Objections

3. Claim 11 is no longer objected to because of the following informality, wherein the claim properly recites biological specimen.

Sequence Compliance

4. This application now contains sequence disclosures within claim 10 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2) and noted to be new matter, hence the objection to the specification is withdrawn, Remarks, page 7.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

5. The rejection of claim 11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicants' amendment to the claim.

Claim Rejections - 35 USC § 102

6. The rejection of claims 3 and 11 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number 2005/0069924 A1 (effective filing date February 23, 2001) is withdrawn in light of Applicants' arguments.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 3, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication number 2005/0069924 A1 (effective filing date February 23, 2001), and further in view of Palmisano et al. (Cancer Research 60: 5954-5958, November 1, 2000/ IDS reference listed on

sheet 4, submitted July 19, 2004) and WO 02/00927 A2 (effective filing date July 2, 2001). The publication teaches a method for detecting a cellular proliferative disorder in a sample from a patient (i.e. plasma, serum, stool, ejaculate, sputum, saliva, cerebrospinal fluid, or blood or a sample embedded in paraffin, tissues, or animal cell membranes of the sample), see abstract and page 8, section 0065.

The publication sets forth inventions including determining, in a nucleic acid-containing specimen taken from a subject, the methylation state of a gene or regulatory sequences associated therewith [(i.e. promoter region)], wherein the methylated regions of the gene and associated regulatory sequences are contained within CpG islands (i.e., CpG rich regions). In the instant case, identification of differentially methylated sequences and CpG islands were recognized in the 5' region of the human B-cell specific transcriptional factor gene PAX5 utilizing bisulfite modification and methylation-specific PCR (MSP). Aberrant methylation typically includes hypermethylation as compared with the same regions of the gene or regulatory sequences in a subject not having the cellular proliferative disorder, see page 3, section 0017; page 5, section 0034; page 13, sections 0099; and page 14, sections 0104- 0106. Absent evidence to the contrary the disclosed PAX5 reads on PAX5 β.

The method of monitoring cancer in the biological specimen included a PCR reaction and amplification methylated templates under a higher annealing temperature, see page 12, section 0097; page 13, section 0099; and page 14, sections 0104 and 0105.

The publication does not "teach a second stage methylation-specific PCR reaction for the PAX5 β3 gene", "…primers sequences for MSP that are specific for the PAX5 β3 gene and likewise no teaching that the temperature of annealing for the primer set is above the melting temperature of the primer set." as asserted by Applicants in the Remarks, see page 7, 1st full paragraph. Applicants are reminded independent claim 3 does not explicitly set forth a specific primer identified by specific sequences or SEQ ID number.

However, Palmisano et al. teaches second stage methylation-specific PCR reaction with the same conditions listed in claim 3, see page 5955, 1st column, MSP section. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention was made to implement the teachings of Palmisano. Palmisano notes "…detection of aberrant promoter region methylation constitutes a promising approach for using DNA-based markers…for…common human cancers" and second stage PCR is art known to increase detection sensitivity and verifies methylation status, see page 5954, paragraph before Materials section. Moreover, the WO document teaches second stage methylation-specific PCR reaction with the same conditions listed in claim 3, as well as primer SEQ ID NO: 3 and SEQ ID NO: 4, see sequence alignment. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention was made to implement the teachings of the WO document, as well as the primers included therein in to critically analyze the methylation status, see pages 15 and 16. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by

both references, see entirety of all documents.

9. Claims 3, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication number 2005/0069924 A1 (effective filing date February 23, 2001), and further in view of WO 02/00927 A2 (effective filing date July 2, 2001). The publication teaches a method for detecting a cellular proliferative disorder in a sample from a patient (i.e. plasma, serum, stool, ejaculate, sputum, saliva, cerebrospinal fluid, or blood or a sample embedded in paraffin, tissues, or animal cell membranes of the sample), see abstract and page 8, section 0065.

The publication sets forth inventions including determining, in a nucleic acid-containing specimen taken from a subject, the methylation state of a gene or regulatory sequences associated therewith [(i.e. promoter region)], wherein the methylated regions of the gene and associated regulatory sequences are contained within CpG islands (i.e., CpG rich regions). In the instant case, identification of differentially methylated sequences and CpG islands were recognized in the 5' region of the human B-cell specific transcriptional factor gene PAX5 utilizing bisulfite modification and methylation-specific PCR (MSP). Aberrant methylation typically includes hypermethylation as compared with the same regions of the gene or regulatory sequences in a subject not having the cellular proliferative disorder, see page 3, section 0017; page 5, section 0034; page 13, sections 0099; and page 14, sections 0104- 0106. Absent evidence to the contrary the disclosed PAX5 reads on PAX5 β.

The method of monitoring cancer in the biological specimen included a PCR reaction and amplification methylated templates under a higher annealing temperature, see page 12, section 0097; page 13, section 0099; and page 14, sections 0104 and 0105.

The publication does not "teach a second stage methylation-specific PCR reaction for the PAX5 β3 gene", and "...primers sequences for MSP that are specific for the PAX5 β3 gene and likewise no teaching that the temperature of annealing for the primer set is above the melting temperature of the primer set" as asserted by Applicants in the Remarks, see page 7, 1st full paragraph. Applicants are reminded independent claim 3 does not explicitly set forth a specific primer identified by specific sequences or SEQ ID number.

However, the WO document teaches second stage methylation-specific PCR reaction with the same conditions listed in claim 3, as well as primers SEQ ID NO: 3 and SEQ ID NO: 4, see sequence alignment. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention was made to implement the teachings of the WO document, as well as the primers included therein in to critically analyze the methylation status, see pages 15 and 16. It is also art known second stage PCR is art known to increase detection sensitivity and verifies methylation status, see page 16. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by both references, see entirety of both documents.

10. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
03 June 2008

/Alana M. Harris, Ph.D./

Primary Examiner, Art Unit 1643